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In vivo deep brain imaging of rats using oral-cavity illuminated photoacoustic computed tomography

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ABSTRACT

We demonstrate, by means of internal light delivery, photoacoustic imaging of the deep brain of rats *in vivo*. With fiber illumination via the oral cavity, we delivered light directly into the bottom of the brain, much more than can be delivered by external illumination. The study was performed using a photoacoustic computed tomography (PACT) system equipped with a 512-element full-ring transducer array, providing a full two-dimensional view aperture. Using internal illumination, the PACT system provided clear cross sectional photoacoustic images from the palate to the middle brain of live rats, revealing deep brain structures such as the hypothalamus, brain stem, and cerebral medulla.

Keywords: oral-cavity illumination; internal illumination; deep brain imaging; photoacoustic computed tomography; optical fiber.

INTRODUCTION

As a nonionizing imaging modality, photoacoustic tomography (PAT) has recently emerged as an important tool in neuroimaging.[1,2] Among the multiple photoacoustic (PA) brain imaging studies reported over the past few years,[3-10] most PA modalities imaged the cortex region due to the limited light penetration depth.[3,5-7,9,10] Thus far, two studies have reported deep brain PA imaging of mice. One study acquired coronal-view images of the brain by using optical fiber bundles illuminating the circumference of the mouse head.[4] However, in the images they presented, the internal brain structures can barely be identified. The other study used external circular illumination through the cranial skull of a dead mouse and identified several deep brain structures,[8] although the dead brain precluded functional neural studies.

Here, we developed a new light delivery scheme facilitating deep brain PA imaging of rats *in vivo*. A multimode optical fiber was inserted into the rat's oral cavity, and the side-illuminated fiber tip delivered more light to the base of the brain than possible with conventional external illumination. The PA signals were collected by a full-ring-array PACT system.

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IMAGING SYSTEM DESIGN

As shown in Figure 1(a), the laser beam (780 nm wavelength, 12 ns pulse width, 10 Hz repetition rate) emitted from a tunable Ti-Sapphire laser (LT-2211A) was first condensed by two convex lenses to a full-width at half-maximum of ~2 mm, and then coupled into a multimode optical fiber (2.8 mm core diameter) with a coupling efficiency of approximately 35 %. The total energy at the fiber output end in the rat's mouth was ~10 mJ. The rat was secured to a holder in an upright position. We then mounted the holder on the translation stage for elevational scans. Figure 1 (b) shows a cross-sectional view of the multimode optical fiber in the rat's mouth. A 45 degree right-angle prism was fixed in an air chamber at the fiber tip, reflecting approximately 60 % of the light toward the palate. The 90 degree bent portion of the fiber was wrapped in aluminum foil to decrease artifacts induced by light leakage.

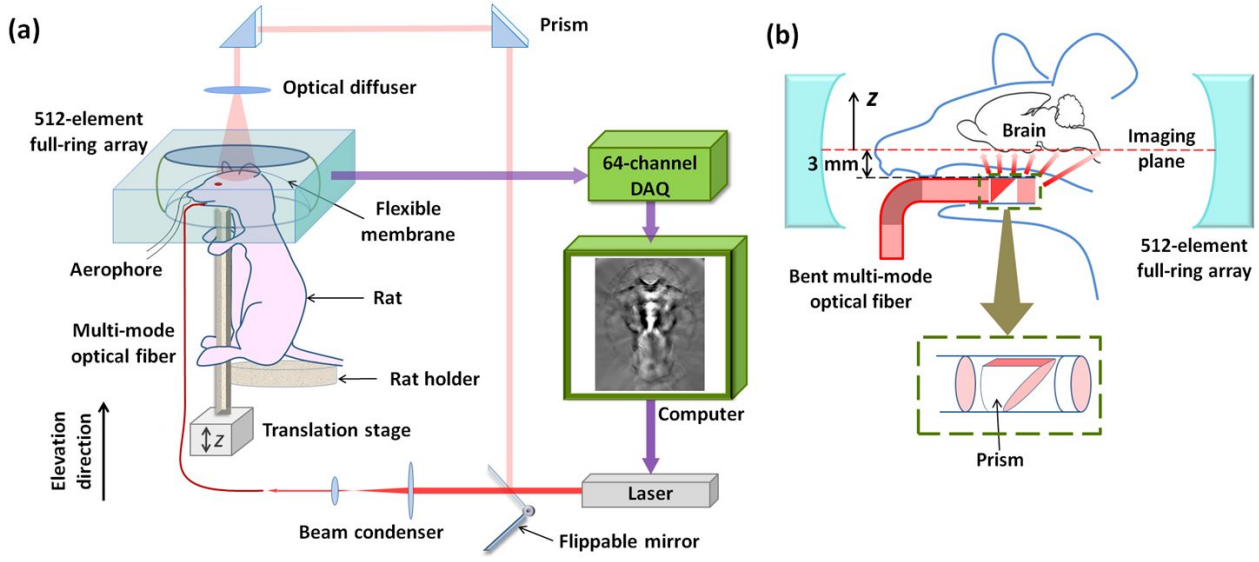

Fig. 1 (a) Schematic of the oral-cavity illuminated photoacoustic computed tomography system. (b) Detailed view of the optical fiber tip in the rat's mouth. The origin of the z-axis is aligned with the imaging plane 3 mm above the fiber tip.

The PACT system utilized a 512-element, 5 MHz transducer array with a 50 mm ring diameter. Within the central imaging region of 20 mm diameter and 1 mm thickness, the system provided ~0.10 mm radial resolution and < 0.25 mm tangential resolution.[9] With pure endogenous hemoglobin contrast, each PA image shown below was acquired with 10 times averaging in 16 s. Previously published papers regarding the same data acquisition system give a detailed description of the hardware.[11,12]

EXPERIMENTAL RESULTS

We imaged the deep brain structures of a healthy outbred rat in order to demonstrate the deep imaging capability provided by internal illumination. After imaging with fiber illumination at various depths, we also redirected the laser light to provide external illumination to acquire a corresponding control image. Figure 2 shows a series of *in vivo* images acquired in the brain's bottom region, with images acquired by internal illumination above [Figs. 2(a)–2(c)] and corresponding images obtained by external illumination below [Figs. 2(d)–2(f)]. Obviously, internal illumination provides much clearer images than external illumination for deep brain imaging.

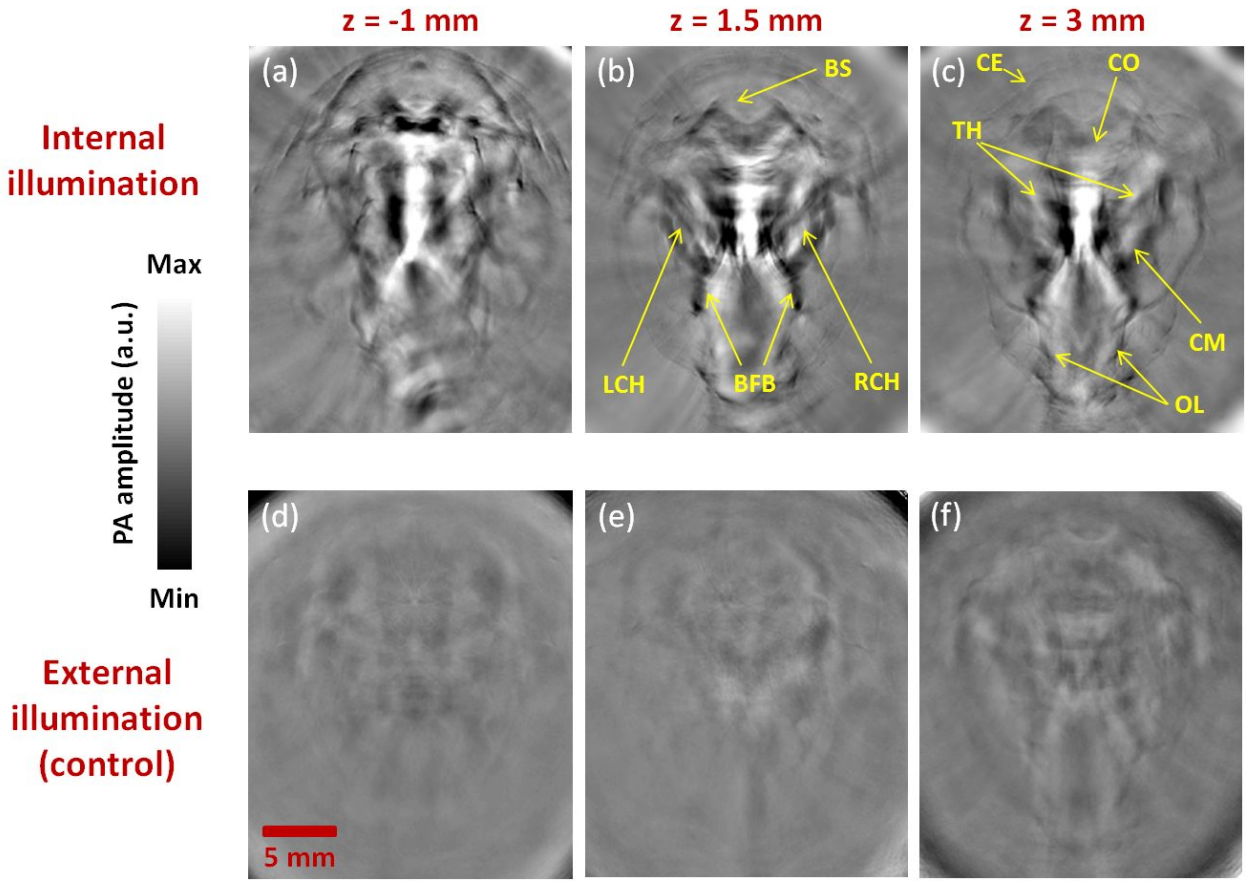

Fig. 2 A series of images acquired at z = –1 mm (a), z = 1.5 mm (b), and z = 3 mm (c), with control images at the same layers (d)–(f) acquired by external illumination through the top skull. BFB, basal forebrain; BS, brain stem; CE, cerebellum; CM, cerebral medulla; CO, colliculus; LCH, left cerebral hemisphere; OL, olfactory lobes; RCH, right cerebral hemisphere; and TH, thalamus.

An *in vivo* PA image of the rat brain base (z = 0 mm, ventral aspect) is shown in Fig. 3 (a). The image clearly reveals the left and right cerebral hemispheres, brain stem, and hypothalamus. The PA image agrees with the anatomical photo shown in Fig. 3(b) well.

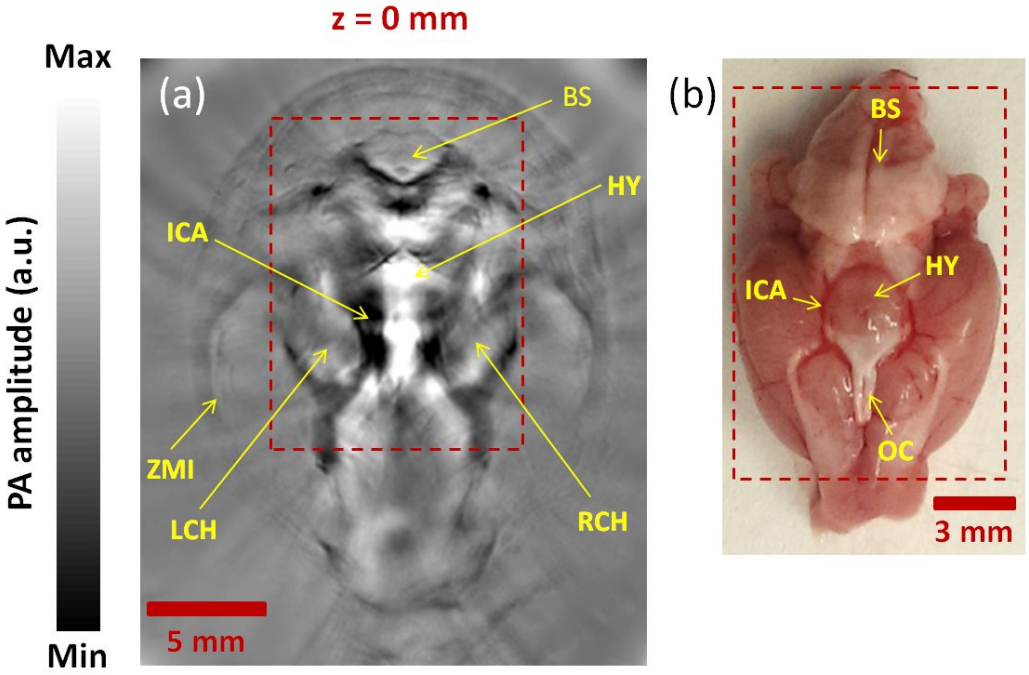

Fig. 3 (a) *In vivo* PA image of the rat brain base (z = 0 mm) acquired by the oral-cavity illuminated photoacoustic computed tomography system. (b) Corresponding photograph of the anatomy of the same rat brain. BS, brain stem; HY, hypothalamus; ICA, internal carotid artery; LCH, left cerebral hemisphere; OC, optic chiasma; RCH, right cerebral hemisphere; and ZMI, zygomatic muscle interface.

CONCLUSION

We have developed a new light delivery scheme utilizing a fiber-transmitted oral-cavity illumination and PACT system to demonstrate the capability of rat deep brain *in vivo* imaging. The scheme can be potentially used to investigate brain blood supply mechanisms, deep brain tumors, and strokes caused by artery occlusion.[13] This illumination method can also be extended to kidney, prostate, and sinus imaging.

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